

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

05.11.2003

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 November 2000 (23.11.2000)

PCT

(10) International Publication Number
WO 00/69456 A3

(51) International Patent Classification⁷: **A61K 39/39**,
39/095, 39/155, 39/21, 39/35, 39/00

(21) International Application Number: PCT/US00/13156

(22) International Filing Date: 12 May 2000 (12.05.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/133,963 13 May 1999 (13.05.1999) US

(71) Applicant (for all designated States except US): **AMERICAN CYANAMID COMPANY** [US/US]; Five Giralda Farms, Madison, NJ 07940 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **HAGEN, Michael** [CA/US]; 12 Summit Oaks, Pittsford, NY 14534 (US).

(74) Agents: **GORDON, Alan, M.**; American Home Products Corporation, Patent Law Dept. - 2B2, One Campus Drive, Parsippany, NJ 07054 et al. (US).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

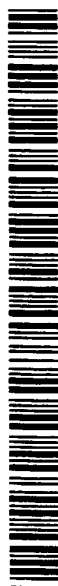
(88) Date of publication of the international search report:
8 February 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ADJUVANT COMBINATION FORMULATIONS

(57) Abstract: The use of 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A and derivatives and analogs thereof, in combination with a cytokine or lymphokine such as granulocyte macrophage colony stimulating factor or interleukin-12 is useful as an adjuvant combination in an antigenic composition to enhance the immune response in a vertebrate host to a selected antigen.

WO 00/69456 A3



ENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

03/05/2000

Applicant's or agent's file reference 33482-00/PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 13156	International filing date (day/month/year) 12/05/2000	(Earliest) Priority Date (day/month/year) 13/05/1999
Applicant AMERICAN CYANAMID COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ **None of the figures.**

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 00/13156

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/39 A61K39/095 A61K39/155 A61K39/21 A61K39/35
A61K39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND, BIOSIS, MEDLINE, CANCERLIT, AIDSLINE, CHEM ABS Data, EMBASE, SCISEARCH, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 57659 A (SMITHKLINE BEECHAM BIOLOG ;BOON THIERRY (BE); SILLA SILVIA (BE); U) 23 December 1998 (1998-12-23)	1,2,4,7, 9,11-15, 18,19, 22,25, 27,40, 41,44, 47,49, 51-53, 55,58, 60,62, 63,66, 67,76, 77,79, 80,82-87
Y	the whole document	3,5,6,8, 10,16, 20,21, 23,24, 26,28,
	--/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

20 November 2000

Date of mailing of the international search report

04/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stein, A

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/US 00/13156

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
		42,43, 45,46, 48,50, 54,56, 57,59, 61,64, 65,68, 69,78,81
Y	--- WO 99 12565 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE); MOMIN PATRICIA MA) 18 March 1999 (1999-03-18) page 4, line 14 - line 23 page 5, line 27 -page 11, line 2 claims 1-4,8-13,17-21 ---	3,8,10, 16,21, 26,28, 43,48, 50,54, 59,61
Y	--- WO 95 29700 A (UNIV DUKE) 9 November 1995 (1995-11-09) cited in the application the whole document ---	20,64, 65,68,69
Y	--- WO 98 56415 A (AQUILA BIOPHARM INC ;UAB RESEARCH FOUNDATION (US)) 17 December 1998 (1998-12-17) page 7, line 31 -page 8, line 11 page 10, line 25 -page 11, line 21 claims 1-20 ---	5,6,23, 24,45, 46,56,57
Y	--- WO 97 28273 A (NORTH AMERICAN VACCINE INC) 7 August 1997 (1997-08-07) the whole document especially page 5 line 29- page 6 line 4 ---	42,78,81
X	--- WO 99 02132 A (CHIRON CORP) 21 January 1999 (1999-01-21) page 12, line 1 -page 16, line 29 page 29, line 23 -page 31, line 33 page 33, line 30 -page 35, line 10 --- -/--	1,3-6, 9-15,18, 21-24, 27-29, 32-35, 38,39, 51, 54-57, 60-63, 66,67, 70,71, 73,74, 82,83, 85,86

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/13156

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	AHLERS J ET AL: "Cytokine-in-adjuvant steering of the immune response phenotype to HIV-1 vaccine constructs: Granulocyte-macrophage colony-stimulating factor and TNF-alpha synergize with IL-12 to enhance induction of cytotoxic T lymphocytes" JOURNAL OF IMMUNOLOGY, vol. 158, 1997, pages 3947-3958, XP002153338 cited in the application page 2W	1-87
A	WO 98 17799 A (WANG BIN ;UNIV PENNSYLVANIA (US); APOLLON INC (US); BOYER JEAN D () 30 April 1998 (1998-04-30) especially page 36 lines 17-34 the whole document	1-87
A	US 5 776 468 A (HAUSER PIERRE ET AL) 7 July 1998 (1998-07-07) the whole document	1-15, 18-87
A	US 5 762 943 A (DOLOVICH JERRY ET AL) 9 June 1998 (1998-06-09) the whole document	16
A	WO 91 16819 A (MOLECULAR RX INC) 14 November 1991 (1991-11-14) the whole document, especially page 9 lines 23-30	17
A	VASLIN BRUNO ET AL: "Induction of humoral and cellular immunity to simian immunodeficiency virus: What are the requirements for protection?" VACCINE, vol. 12, no. 12, 1994, pages 1132-1140, XP002153339 ISSN: 0264-410X the whole document	29-39, 70-75
P,X	WO 99 40937 A (AMERICAN CYANAMID CO) 19 August 1999 (1999-08-19) the whole document	1-14, 51-61, 82-87
P,X	WO 99 27944 A (SCHENK DALE B ;ATHENA NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) the whole document	1-14,17

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 00/13156

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 11-17 and 62-87 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/13156

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9857659 A	23-12-1998	WO 9857660 A EP 1001808 A EP 0977589 A	23-12-1998 24-05-2000 09-02-2000
WO 9912565 A	18-03-1999	AU 9623898 A EP 1009430 A	29-03-1999 21-06-2000
WO 9529700 A	09-11-1995	AU 707894 B AU 2372695 A CA 2189045 A EP 0762895 A JP 9512561 T US 5993819 A	22-07-1999 29-11-1995 09-11-1995 19-03-1997 16-12-1997 30-11-1999
WO 9856415 A	17-12-1998	EP 0988053 A	29-03-2000
WO 9728273 A	07-08-1997	AU 2115897 A EP 0877816 A HU 9901039 A NO 983474 A PL 328096 A	22-08-1997 18-11-1998 28-07-1999 30-09-1998 04-01-1999
WO 9902132 A	21-01-1999	AU 8298298 A EP 1006999 A	08-02-1999 14-06-2000
WO 9817799 A	30-04-1998	AU 5002297 A BR 9712852 A EP 0958364 A	15-05-1998 16-11-1999 24-11-1999
US 5776468 A	07-07-1998	AU 685443 B AU 6426494 A BR 9405957 A DE 69405551 D DE 69405551 T EP 0689454 A FI 954514 A GR 3025483 T JP 8508722 T NO 953759 A PL 310598 A SK 117395 A AP 515 A AT 157882 T AU 705739 B AU 7541696 A CA 2157376 A CN 1119829 A CZ 9502467 A DK 689454 T WO 9421292 A EP 0812593 A ES 2109685 T HU 72916 A IL 109056 A NZ 263538 A SG 48309 A ZA 9401957 A	22-01-1998 11-10-1994 12-12-1995 16-10-1997 26-03-1998 03-01-1996 22-09-1995 27-02-1998 17-09-1996 22-09-1995 27-12-1995 06-11-1996 09-08-1996 15-09-1997 03-06-1999 13-02-1997 29-09-1994 03-04-1996 13-03-1996 08-12-1997 29-09-1994 17-12-1997 16-01-1998 28-06-1996 15-06-1998 28-10-1996 17-04-1998 31-01-1995

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/13156

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5762943 A	09-06-1998	AU 3121497 A CA 2252604 A EP 0914114 A WO 9742947 A	05-12-1997 20-11-1997 12-05-1999 20-11-1997
WO 9116819 A	14-11-1991	AT 153534 T CA 2081482 A DE 69126304 D DE 69126304 T EP 0526511 A JP 2980677 B JP 6502387 T US 5851996 A US 5753624 A	15-06-1997 28-10-1991 03-07-1997 04-09-1997 10-02-1993 22-11-1999 17-03-1994 22-12-1998 19-05-1998
WO 9940937 A	19-08-1999	AU 2596699 A	30-08-1999
WO 9927944 A	10-06-1999	BR 9815357 A EP 1033996 A NO 20002784 A AU 1706199 A	24-10-2000 13-09-2000 31-07-2000 16-06-1999